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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,167	07/27/2001	Nancy L. Paiva	11137/04704	7718

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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,167	PAIVA ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,21-42 and 58-67* is/are pending in the application.

4a) Of the above claim(s) *31-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,21-30,34-42 and 58-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

STATUS OF THE APPLICATION

1. This Office action is in response to the Amendment and Remarks filed 1 December 2003.

2. Claims 19, 20 and 43-57 have been cancelled.

3. Claims 31-33 remain withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed 5 November 2002.

4. This application contains claims 31-33 drawn to an invention nonelected without traverse in the response filed 5 November 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR § 1.144), see MPEP § 821.01.

5. The rejection under 35 U.S.C. § 112, first paragraph for enablement of claims 3-7, 10-14, 17, 18, 21-26, 28, 30, 35-38, 40 and 42 is withdrawn in view of Applicant's explanation of the issued on pages 12-14 of the Remarks.

6. The rejection under 35 U.S.C. § 103(a) over Hain *et al* in view of Comai *et al* is withdrawn in favor of the rejection below which is more pertinent to the claimed invention and the teachings of the instant application, the arguments have been essentially addressed herein.

7. Those rejections or objections not specifically addressed in this Office action are withdrawn in view of Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112

8. Claims 27, 28, 34-38, 41 and 42 remain rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 14 January 2003. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive.

At claims 27, 34 and 41, as directed to the limitation "under conditions conductive to the accumulation of..." Applicant argues that that the transgenic plant cells are cultivated under conditions conducive to the accumulation of p-coumaryl CoA and malonyl CoA and that both p-coumaryl CoA and malonyl CoA are known precursors of many metabolites in plants, including phenylpropanoids, flavonoids, lignin and fatty acids, and conditions conducive to the accumulation of these precursors are well known in the art for all precursors to include keeping the plants in a healthy non-stressed state. Applicant argues that the specification discloses the accumulation of resveratrol glucoside is favored in non-stressed tissues and that this limitation is defined in the specification and by common knowledge of one skilled in the art (pages 10-11 of the Remarks). The arguments put forth by Applicant as directed to additional rejection of claim 34 on pages 11-12 of the Remarks are essentially the same and addressed below. These arguments are not found to be persuasive because it is unclear from the specification, and the art, how one of skill in the art is to practice such a cultivating step to keep the plants in a healthy non-stressed state in order to practice the claimed

invention. In addition, the limitation "to minimizing the concentration of β-glucosidase active on resveratrol glucoside" is in an improper grammatical form and is indefinite because it is unclear what the metes and bounds of this limitation are in the claims as amended. Even though it may be know in the art the release of β-glucosides in plant cells due to stresses such as fungal infection, UV damage or wounding decrease the amount of precursors for resveratrol glucoside syntheses, these facts do not specifically teach the metes and bounds of the conditions that are conductive to the accumulation of precursors *per se*.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 1, 2, 15, 16, 24-27, 29, 34, 39, 41 and 67 are rejected under 35 U.S.C. § 102(b) as being anticipated by Leekband and Lorz (Theoretical and Applied Genetics June 1998, 96:1004-1012).

Leekband and Lorz disclose edible plant material suitable for consumption as a food stuff that being barley and wheat, comprising transgenic plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter, and a method of making said edible plant material (Table 1 on page 1009). Leekband and Lorz disclose seed and progeny from said seed (Table 1 on page 1009). Consuming said barely or wheat would be an inherent use of said barely or wheat. Leekband and

Lorz disclose a method of increasing disease resistance in said plant(s) and spoilage (Figure 6 on page 1010). In Applicant's response as directed to the rejections under 35 USC § 103, Applicant argues that the prior art does not suggest or teach the accumulation of resveratrol glucoside in such plants. While Leekband and Lorz are silent as to the production of resveratrol glucoside, without evidence to the contrary, the transformed barley or wheat plant disclosed by Leekband and Lorz would inherently accumulate resveratrol glucoside as Applicant claims.

The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same, material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the Applicant to provide that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

See *Integra LifeSciences I Ltd. v. Merck KGaA* 50 USPQ2d 1846, 1850 (DC SCalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then the prior art anticipates the claimed method.

Claim Rejections - 35 USC § 103

11. Claims 1, 2, 5-9, 12-16, 21-27, 29, 34, 36-39 and 41 remain rejected and claims 3, 4 10, 11, 17, 18, 28, 30-33, 35, 40, 42 and 58-67 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Schroder *et al* (U.S. Patent 5,689,046 issued 18

November 1997) in view of Comai *et al* (U.S. Patent 5,106,739) and further in view of Tropf *et al* (1994, J. Mol. Evol. 38:610-618), Leekband and Lorz (Theoretical and Applied Genetics June 1998, 96:1004-1012) and Applicant's admission. This rejection is repeated for the reason of record as set forth in the last Office action mailed 14 January 2003, and has been modified to include claims directed to plants and methods comprising a transgene encoding the specific amino acid sequence of SEQ ID NO: 2 and new claims 58-67. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive.

The teachings of Schroder *et al* and Comai *et al* can be found in the previous Office action.

Tropf *et al* teach a transgene encoding the amino acid sequence of SEQ ID NO: 2 having resveratrol synthase activity produced from a nucleic acid isolated from peanut (*Arachis hypogaea*) (page 611, right column, last paragraph). Applicant has admitted in the response to the rejection under 35 U.S.C. § 112, first paragraph, for enablement that the transgene taught by Tropf *et al* encodes the amino acid sequence of SEQ ID NO: 2 (pages 12-14 of the Remarks).

Leekband and Lorz teach that it was obvious to one of ordinary skill in the art at the time of Applicant's invention to operably link a constitutive promoter to a resveratrol synthase transgene and transform a plant.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Schroder *et al* to substitute the transgene encoding Applicant's SEQ ID NO: 2 as taught by Tropf *et al* and use the

constitutive promoter taught by Comai *et al* and additionally suggested by Leekband and Lorz. Schroder *et al* motivates one of ordinary skill in the art to use transgenes encoding peanut resveratrol synthase (syn. stilbene synthase) at claims 7 and 14. In addition, Schroder *et al* teaches that other, "foreign" regulatory parts can be arranged upstream of the structural gene (column 4, lines 32-36). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to use a constitutive promoter such as that taught by Comai *et al* and Leekband and Lorz to increase resveratrol in a transformed plant in a constitutive manner, and one of ordinary skill in the art would have had a reasonable expectation of success.

Applicant argues that Comai teaches high levels of expression of coding sequences obtained by using CAMV 35S enhanced MAS promoter in plant cells but does not teach or suggest its use in transformation of plants with a stilbene synthase gene (page 14, last paragraph of the Remarks). This argument is not found to be persuasive because Comai teaches that one of ordinary skill in the art at the time of Applicant's invention would have motivated to use a constitutive promoter when transforming a plant with a transgene in general.

Applicants argue that when the teachings of Schroder are combined with a constrictive promoter as taught by Comai, the predicted result based on his patent and earlier publication would be free resveratrol constitutively produced in transgenic plants and that there is nothing in either Schroder or Comai singly or combined that suggests the accumulation of resveratrol glucoside in a somewhat tissue-specific manner as demonstrated in the present invention. Applicants also argue that there is nothing in

Schroder or Comai, singly or combined, that would lead someone skilled in the art to contemplate that when a plant which does not contain an endogenous resveratrol synthase gene is transformed with a resveratrol synthase gene or cDNA, an endogenous glucosyl transferase would be able to interact with the product of the resveratrol synthase transgene to form resveratrol glucoside and that Schroder or Comai, singly or combined, also do not teach the increased nutritional or nutraceutical value obtained by the unexpected accumulation of resveratrol glucoside in plants expressing a resveratrol synthase gene under the control of a constitutive promoter (page 15, 2nd paragraph of the Remarks). These arguments are not found to be persuasive because the instant specification and claims do not teach a manipulative difference from that previously suggested in the prior art or that would have been obvious to one of ordinary skill in the art at the time of Applicant's invention. Schroder *et al* teach that it is desirable to introduce the resveratrol synthase gene into alfalfa and soybean as exemplified by Applicant (column 6, line 16). In such an instance, the alfalfa or soybean would naturally produce resveratrol glucoside without further manipulation by one of ordinary skill in the art, and alfalfa and soybean were well know in the art at the time of Applicant's invention as a desirable edible plant materials for both humans and animals.

Applicants argue that they have shown that transforming plant cells with a resveratrol synthase transgene under the control of a constitutive promoter results in the accumulation of not resveratrol, but instead resveratrol glucoside upon expression of the resveratrol synthase transgene and that they have shown that the resveratrol

glucoside formation is tissue-specific with high accumulation in young leaves and old internodes of transformed alfalfa. Applicants argue that they have also shown that accumulation of resveratrol glucoside is favored in plant tissues which contain the necessary biosynthetic precursors and low levels of β-glucosidases, and that such conditions may be found in any plant cell, but are more likely to be present in non-stressed tissues, such as leaves constantly expressing a resveratrol synthase coding region driven by a constitutive promoter, rather than wounded or infected tissues which contain, release, or induce β-glucosidases and that Schroder, either alone or combined with Comai, does not teach or suggest that transforming a plant with resveratrol synthase results in the accumulation of resveratrol glucoside as taught by the present invention. The arguments are not found to be persuasive, because as previously stated the claims do not teach a manipulative difference in the transgenic plants beyond what has been previously suggested in the prior art. The methods of use are deemed obvious because the transformed plants suggested by the prior art are known edible plant material, and the intended use as a nutritional or nutraceutical does not teach a patentable difference from the obvious use of the transformed plants suggested by the prior art. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as

compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Conclusion

12. This Office action is non-final.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

David M Kruse
AU 1638

David H. Kruse, Ph.D.
8 March 2004